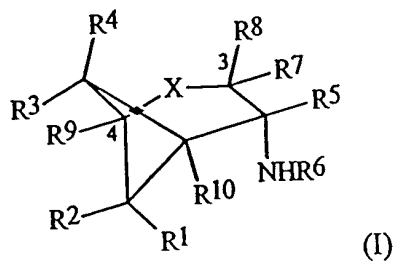


## CLAIMS

What is claimed is:

1. A compound of formula I:



wherein

$R^1, R^2, R^3, R^4, R^7, R^8, R^9$ , and  $R^{10}$  are each independently hydrogen, carboxy, tetrazolyl,  $-SO_2OH$ ,  $-PO(OH)_2$ ,  $-B(OH)_2$ ,  $(C_1-C_6)alkyl$ ,  $(C_3-C_6)cycloalkyl$ ,  $(C_3-C_6)cycloalkyl(C_1-C_6)alkyl$ ,  $(C_2-C_6)alkenyl$ ,  $(C_2-C_6)alkynyl$ ,  $(C_1-C_6)alkoxy$ , halo $(C_1-C_6)alkyl$ , hydroxy $(C_1-C_6)alkyl$ ,  $(C_1-C_6)alkanoyl$ ,  $(C_1-C_6)alkanoyloxy$ ,  $(C_1-C_6)alkoxycarbonyl$ , cyano, halo,  $-CONR_aR_b$ ,  $-NR_cR_d$ ,  $-SR_e$ , aryl, heteroaryl, aryl $(C_1-C_6)alkyl$ , diaryl $(C_1-C_6)alkyl$ , or heteroaryl $(C_1-C_6)alkyl$ , wherein any aryl or heteroaryl may optionally be substituted with 1, 2 or 3 substituents selected from the group consisting of halo, hydroxy,  $(C_1-C_6)alkoxy$ ,  $(C_1-C_6)alkyl$ ,  $(C_3-C_6)cycloalkyl$ ,  $(C_3-C_6)cycloalkyl(C_1-C_6)alkyl$ ,  $(C_1-C_6)alkanoyl$ ,  $(C_1-C_6)alkanoyloxy$ ,  $(C_1-C_6)alkoxycarbonyl$ , cyano, nitro, trifluoromethyl, trifluoromethoxy, and carboxy;

$R^5$  is carboxy, tetrazolyl,  $(C_1-C_6)alkoxycarbonyl$ ,  $-SO_2OH$ ,  $-B(OH)_2$ , or  $-PO(OH)_2$ ;

$R^6$  is hydrogen,  $(C_1-C_6)alkyl$ ,  $(C_3-C_6)cycloalkyl$ ,  $(C_3-C_6)cycloalkyl(C_1-C_6)alkyl$ , aryl, aryl $(C_1-C_6)alkyl$ , heteroaryl, heteroaryl $(C_1-C_6)alkyl$ ,  $(C_1-C_6)alkoxycarbonyl$ , or  $(C_1-C_6)alkanoyl$ ;

X is absent (a direct or single bond connects C<sub>3</sub> and C<sub>4</sub>), oxy (-O-), thio (-S-), sulfinyl (-SO-), sulfonyl (-SO<sub>2</sub>-), -C(R<sub>d</sub>)(R<sub>e</sub>)-, seleno (-Se-), -P(R<sub>d</sub>)-, or -N(R<sub>x</sub>)-, wherein R<sub>x</sub> is hydrogen, (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>1</sub>-C<sub>6</sub>)alkanoyl, aryl, aryl(C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonyl, or aryl(C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonyl;

each R<sub>a</sub>, R<sub>b</sub> and R<sub>c</sub> is independently hydrogen, (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl, (C<sub>2</sub>-C<sub>6</sub>)alkenyl, (C<sub>2</sub>-C<sub>6</sub>)alkynyl, aryl, heteroaryl, benzyl, or phenethyl;

each R<sub>c</sub> or R<sub>d</sub> is independently hydrogen, (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl, (C<sub>2</sub>-C<sub>6</sub>)alkenyl, (C<sub>2</sub>-C<sub>6</sub>)alkynyl, (C<sub>1</sub>-C<sub>6</sub>)alkanoyl, aryl, heteroaryl, benzyl, or phenethyl; or R<sub>c</sub> and R<sub>d</sub> together with the nitrogen to which they are attached are triazolyl, imidazolyl, oxazolidinyl, isoxazolidinyl, pyrrolyl, morpholino, piperidino, pyrrolidino, pyrazolyl, indolyl, or tetrazolyl;

R<sub>f</sub> and R<sub>g</sub> are each independently hydrogen, carboxy, (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl(C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>2</sub>-C<sub>6</sub>)alkenyl, (C<sub>2</sub>-C<sub>6</sub>)alkynyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, halo(C<sub>1</sub>-C<sub>6</sub>)alkyl, hydroxy(C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>1</sub>-C<sub>6</sub>)alkanoyl, (C<sub>1</sub>-C<sub>6</sub>)alkanoyloxy, (C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonyl, cyano, halo, -CONR<sub>h</sub>R<sub>i</sub>, -NR<sub>j</sub>R<sub>k</sub>, -SR<sub>m</sub>, aryl, heteroaryl, aryl(C<sub>1</sub>-C<sub>6</sub>)alkyl, or heteroaryl(C<sub>1</sub>-C<sub>6</sub>)alkyl, wherein any aryl or heteroaryl may optionally be substituted with 1, 2 or 3 substituents selected from the group consisting of halo, hydroxy, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl(C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>1</sub>-C<sub>6</sub>)alkanoyl, (C<sub>1</sub>-C<sub>6</sub>)alkanoyloxy, (C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonyl, cyano, nitro, trifluoromethyl, trifluoromethoxy, and carboxy; or R<sub>f</sub> and R<sub>g</sub> together are oxo (=O) or thioxo (=S);

each R<sub>h</sub>, R<sub>i</sub>, and R<sub>m</sub> is independently hydrogen, (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl, (C<sub>2</sub>-C<sub>6</sub>)alkenyl, (C<sub>2</sub>-C<sub>6</sub>)alkynyl, aryl, heteroaryl, benzyl, or phenethyl; and

each R<sub>j</sub> or R<sub>k</sub> is independently hydrogen, (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl, (C<sub>2</sub>-C<sub>6</sub>)alkenyl, (C<sub>2</sub>-C<sub>6</sub>)alkynyl, (C<sub>1</sub>-C<sub>6</sub>)alkanoyl, aryl, heteroaryl, benzyl, or phenethyl; or R<sub>j</sub> and R<sub>k</sub> together with the nitrogen to which they are attached are triazolyl, imidazolyl, oxazolidinyl, isoxazolidinyl, pyrrolyl, morpholino, piperidino, pyrrolidino, pyrazolyl, indolyl, or tetrazolyl;

or a pharmaceutically acceptable salt or prodrug thereof;  
wherein at least one of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>9</sup>, and R<sup>10</sup> is carboxy,  
tetrazolyl, -SO<sub>2</sub>OH, -PO(OH)<sub>2</sub>, or -B(OH)<sub>2</sub>.

2. The compound of claim 1 wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, and R<sup>10</sup> are each independently hydrogen, carboxy, tetrazolyl, -SO<sub>2</sub>OH, -PO(OH)<sub>2</sub>, (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl(C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>1</sub>-C<sub>6</sub>)alkanoyl, cyano, halo, -NR<sub>c</sub>R<sub>d</sub>, aryl, heteroaryl, aryl(C<sub>1</sub>-C<sub>6</sub>)alkyl, diaryl(C<sub>1</sub>-C<sub>6</sub>)alkyl, or heteroaryl(C<sub>1</sub>-C<sub>6</sub>)alkyl, wherein any aryl or heteroaryl may optionally be substituted with 1, 2 or 3 substituents selected from the group consisting of halo, hydroxy, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl(C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>1</sub>-C<sub>6</sub>)alkanoyl, (C<sub>1</sub>-C<sub>6</sub>)alkanoyloxy, (C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonyl, cyano, nitro, trifluoromethyl, trifluoromethoxy, and carboxy.

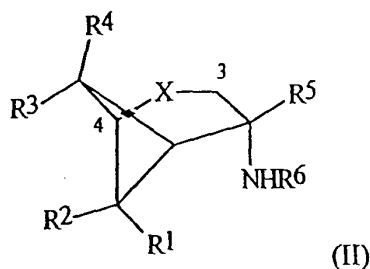
3. The compound of claim 1 wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, and R<sup>10</sup> are each independently hydrogen, carboxy, tetrazolyl, (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, (C<sub>1</sub>-C<sub>6</sub>)alkanoyl, cyano, halo, aryl, or heteroaryl, wherein any aryl or heteroaryl may optionally be substituted with 1, 2 or 3 substituents selected from the group consisting of halo, hydroxy, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>1</sub>-C<sub>6</sub>)alkanoyl, (C<sub>1</sub>-C<sub>6</sub>)alkanoyloxy, (C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonyl, cyano, nitro, trifluoromethyl, trifluoromethoxy, and carboxy.

4. The compound of claim 1 wherein R<sup>5</sup> is carboxy, tetrazolyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonyl, -SO<sub>2</sub>OH, or -PO(OH)<sub>2</sub>.

5. The compound of claim 1 wherein R<sup>5</sup> is carboxy.

6. The compound of claim 1 wherein R<sup>6</sup> is hydrogen, (C<sub>1</sub>-C<sub>6</sub>)alkyl, aryl, aryl(C<sub>1</sub>-C<sub>6</sub>)alkyl, diaryl(C<sub>1</sub>-C<sub>6</sub>)alkyl, or (C<sub>1</sub>-C<sub>6</sub>)alkanoyl.

7. The compound of claim 1 wherein X is absent.
8. The compound of claim 1 wherein X is oxy, thio, sulfinyl, sulfonyl or  $-N(R_X)-$ .
9. The compound of claim 1 wherein X is  $-C(R_c)(R_g)-$ .
10. A compound of formula II:



wherein

$R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$ , are each independently hydrogen, carboxy, tetrazolyl,  $-SO_2OH$ ,  $-PO(OH)_2$ ,  $(C_1-C_6)$ alkyl,  $(C_3-C_6)$ cycloalkyl,  $(C_3-C_6)$ cycloalkyl $(C_1-C_6)$ alkyl,  $(C_2-C_6)$ alkenyl,  $(C_2-C_6)$ alkynyl,  $(C_1-C_6)$ alkoxy, halo $(C_1-C_6)$ alkyl, hydroxy $(C_1-C_6)$ alkyl,  $(C_1-C_6)$ alkanoyl,  $(C_2-C_6)$ alkanoyloxy,  $(C_1-C_6)$ alkoxycarbonyl, cyano, halo,  $-CONR_aR_b$ ,  $-NR_cR_d$ ,  $-SR_e$ , aryl, heteroaryl, aryl $(C_1-C_6)$ alkyl, or heteroaryl $(C_1-C_6)$ alkyl, wherein any aryl or heteroaryl may optionally be substituted with 1, 2 or 3 substituents selected from the group consisting of halo, hydroxy,  $(C_1-C_6)$ alkoxy,  $(C_1-C_6)$ alkyl,  $(C_3-C_6)$ cycloalkyl,  $(C_3-C_6)$ cycloalkyl $(C_1-C_6)$ alkyl,  $(C_1-C_6)$ alkanoyl,  $(C_1-C_6)$ alkanoyloxy,  $(C_1-C_6)$ alkoxycarbonyl, cyano, nitro, trifluoromethyl, trifluoromethoxy, and carboxy;

$R^5$  is carboxy, tetrazolyl,  $(C_1-C_6)$ alkoxycarbonyl,  $-SO_2OH$  or  $-PO(OH)_2$ ;

$R^6$  is hydrogen,  $(C_1-C_6)$ alkyl,  $(C_3-C_6)$ cycloalkyl,  $(C_3-C_6)$ cycloalkyl $(C_1-C_6)$ alkyl, phenyl, benzyl,  $(C_1-C_6)$ alkoxycarbonyl,  $(C_1-C_6)$ alkanoyl, or phenethyl;

X is absent, oxy (-O-), thio (-S-), sulfinyl (-SO-), sulfonyl (-SO<sub>2</sub>-), -C(R<sub>f</sub>)(R<sub>g</sub>)-, or -N(R<sub>x</sub>)-, wherein R<sub>x</sub> is hydrogen,  $(C_1-C_6)$ alkyl,  $(C_1-C_6)$ alkanoyl, phenyl, benzyl, or benzyloxycarbonyl;

each R<sub>a</sub>, R<sub>b</sub>, and R<sub>c</sub> is independently hydrogen,  $(C_1-C_6)$ alkyl,  $(C_3-C_6)$ cycloalkyl,  $(C_2-C_6)$ alkenyl,  $(C_2-C_6)$ alkynyl, aryl, heteroaryl, benzyl, or phenethyl;

each R<sub>e</sub> or R<sub>d</sub> is independently hydrogen,  $(C_1-C_6)$ alkyl,  $(C_3-C_6)$ cycloalkyl,  $(C_2-C_6)$ alkenyl,  $(C_2-C_6)$ alkynyl,  $(C_1-C_6)$ alkanoyl, aryl, heteroaryl, benzyl, or phenethyl; or R<sub>e</sub> and R<sub>d</sub> together with the nitrogen to which they are attached are triazolyl, imidazolyl, oxazolidinyl, isoxazolidinyl, pyrrolyl, morpholino, piperidino, pyrrolidino, pyrazolyl, indolyl, or tetrazolyl;

R<sub>f</sub> and R<sub>g</sub> are each independently hydrogen, carboxy,  $(C_1-C_6)$ alkyl,  $(C_3-C_6)$ cycloalkyl,  $(C_3-C_6)$ cycloalkyl $(C_1-C_6)$ alkyl,  $(C_2-C_6)$ alkenyl,  $(C_2-C_6)$ alkynyl,  $(C_1-C_6)$ alkoxy, halo $(C_1-C_6)$ alkyl, hydroxy $(C_1-C_6)$ alkyl,  $(C_1-C_6)$ alkanoyl,  $(C_2-C_6)$ alkanoyloxy,  $(C_1-C_6)$ alkoxycarbonyl, cyano, halo, -CONR<sub>h</sub>R<sub>i</sub>, -NR<sub>j</sub>R<sub>k</sub>, or -SR<sub>m</sub>, aryl, heteroaryl, aryl $(C_1-C_6)$ alkyl, or heteroaryl $(C_1-C_6)$ alkyl, wherein any aryl or heteroaryl may optionally be substituted with 1, 2 or 3 substituents selected from the group consisting of halo, hydroxy,  $(C_1-C_6)$ alkoxy,  $(C_1-C_6)$ alkyl,  $(C_3-C_6)$ cycloalkyl,  $(C_3-C_6)$ cycloalkyl $(C_1-C_6)$ alkyl,  $(C_1-C_6)$ alkanoyl,  $(C_1-C_6)$ alkanoyloxy,  $(C_1-C_6)$ alkoxycarbonyl, cyano, nitro, trifluoromethyl, trifluoromethoxy, and carboxy; or R<sub>f</sub> and R<sub>g</sub> together are oxo (=O) or thioxo (=S);

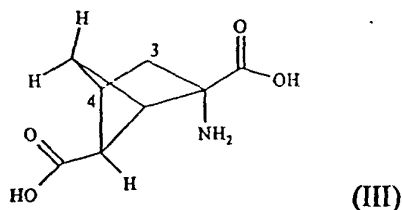
each R<sub>h</sub>, R<sub>i</sub>, and R<sub>m</sub> is independently hydrogen,  $(C_1-C_6)$ alkyl,  $(C_3-C_6)$ cycloalkyl,  $(C_2-C_6)$ alkenyl,  $(C_2-C_6)$ alkynyl, aryl, heteroaryl, benzyl, or phenethyl; and

each R<sub>j</sub> or R<sub>k</sub> is independently hydrogen,  $(C_1-C_6)$ alkyl,  $(C_3-C_6)$ cycloalkyl,  $(C_2-C_6)$ alkenyl,  $(C_2-C_6)$ alkynyl,  $(C_1-C_6)$ alkanoyl, aryl, heteroaryl, benzyl, or phenethyl; or R<sub>j</sub> and R<sub>k</sub> together with the nitrogen to which they are

attached are triazolyl, imidazolyl, oxazolidinyl, isoxazolidinyl, pyrrolyl, morpholino, piperidino, pyrrolidino, pyrazolyl, indolyl, or tetrazolyl;  
 or a pharmaceutically acceptable salt thereof;  
 wherein at least one of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> is carboxy, tetrazolyl, or -SO<sub>2</sub>OH.

11. The compound of claim 10 wherein wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup>, are each independently hydrogen, carboxy, tetrazolyl, -SO<sub>2</sub>OH, (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl(C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, halo(C<sub>1</sub>-C<sub>6</sub>)alkyl, hydroxy(C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>1</sub>-C<sub>6</sub>)alkanoyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonyl, phenyl, benzyl, benzyloxy, phenethyl, cyano, mercapto, (C<sub>1</sub>-C<sub>6</sub>)alkylthio, or halo; R<sup>5</sup> is carboxy, tetrazolyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonyl, or -SO<sub>2</sub>OH; and R<sup>6</sup> is hydrogen, (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl(C<sub>1</sub>-C<sub>6</sub>)alkyl, phenyl, benzyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonyl, (C<sub>1</sub>-C<sub>6</sub>)alkanoyl, or phenethyl; and X is absent.



12. The compound of claim 10 which is a compound of formula III:



or a pharmaceutically acceptable salt or prodrug thereof.

13. A pharmaceutical composition comprising a compound of claim 1 in combination with a pharmaceutically acceptable carrier.

14. A therapeutic method for preventing or treating a pathological condition or symptom in a mammal which is associated with abnormal activity of a



metabotropic glutamate receptor, comprising administering to a mammal in need of such therapy, an effective amount of a compound of claim 1.

15. The method of claim 14 wherein the condition is, or the symptom is associated with epilepsy, cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, pain, spinal cord injury, head trauma, perinatal hypoxia, cardiac arrest and hypoglycemic damage, anxiety, neurodegenerative diseases, Huntington's Chorea, AIDS-induced dementia, ocular damage, retinopathy, cognitive disorders, Parkinson's Disease, or Multiple Sclerosis.

16. The method of claim 14 wherein the condition results in progressive loss of neuronal cells and/or cellular function.

17. The method of claim 14 wherein the condition is, or the symptom is associated with stroke.

18. The method of claim 14 wherein the condition is, or the symptom is associated with Alzheimer's disease.

19. A therapeutic method to treat or manage an addiction comprising administering an effective amount of a compound of claim 1 to a mammal in need of such therapy.

20. The compound of claim 1 comprising a detectable label.